

reaction vessel without the need for purification steps such as phenol extraction followed by precipitation. The amendments to claim 20 are necessitated by the amendments to claim 1.

Applicants respectfully request reconsideration of the pending rejections and reexamination of the present claims in light of the amendments and the remarks detailed below. It is submitted that no new matter has been introduced by the present amendments and entry of the same is respectfully requested.

By these amendments, Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q. 2d 1865 (U.S. 1997); and *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 122 S.Ct. 1831 2002 WL 1050479 U.S..

#### ***Amendments Entered***

Applicants note that an amendment filed 02/08/2002 has been entered and thank the examiner.

#### ***Non-statutory Double Patenting***

The Examiner has maintained the provisional obviousness-type double patenting rejection of claims 5-8 and 10-22, over claims 1-17, 24-43, and 50-69 of copending Application Ser. No. 09/285,658. See, paper No. 17 at pages 2-3, paragraph 3. Applicants respectfully traverse this rejection. Without acquiescing to the rejections, and because these rejections are provisional, Applicants respectfully request that the rejections be held in abeyance until a patent may issue from copending Application Ser. No. 09/285,658.

#### ***Withdrawn Rejections***

Applicants acknowledge and thank the Examiner for withdrawing the rejection of claims 1, 3-13, and 20-25 under 35 U.S.C. §112, second paragraph because of the previous amendment.

#### ***Anticipation Rejection Under 35 U.S.C. §102(b)***

The Examiner rejected claims 1, 3-7 and 22-25 under 35 U.S.C. §102(b) over Sooknanan *et. al.* (WO96/17079). See paper No. 17 at page 7, paragraph 4. Applicants respectfully traverse this rejection.

The invention in Sooknanan *et al.* “is a method for amplifying a specific nucleic acid sequence, at a relatively constant temperature and without serial addition of reagents.” (*See*, page 6 lines 4-5, emphasis added). As amended, the presently claimed invention relates to a method for amplification of a population of nucleic acids with serial addition of reagents. The presently claimed method amplifies RNAs that comprise a poly(A) tail by hybridizing a primer comprising oligo-(dT) to a population of poly(A)+ RNA. The method of Sooknanan *et al.* uses a primer that is designed to specifically hybridize to and amplify a single template sequence. In addition, Sooknanan *et al.* does not disclose the sequential addition of enzymes and buffers. The sequential addition of enzymes and buffers in the presently claimed invention allows for a change of buffer conditions at each subsequent step which allows for optimization of conditions for the enzymes being added at each subsequent step. This further allows for the separation of the first strand cDNA synthesis step and the second strand cDNA synthesis step. Sooknanan *et al.* combines synthesis of first and second strand cDNA with synthesis of RNA. Consequently, Applicants assert that Sooknanan *et. al.* does not show or suggest the presently claimed invention as Sooknanan *et. al.* does not amplify a population of nucleic acids as specified in claim 1 and does not teach serial addition of reagents. Therefore, this rejection should be withdrawn.

The examiner also rejected new claim 26 over Sooknanan *et al.* stating that “there is no limitation in the claim language on what is temperature range for the thermal stable polymerase”. Thermal stable polymerases are well known in the art to be functional at higher temperatures than non-thermal stable polymerases, for example, the 20 minute incubation at 75°C on page 14, line 1 of the specification.

***Obviousness Rejection Under 35 U.S.C. §103(a)-Sooknanan et. al. in view of Kwoh et. al. and Goller et. al.***

The Examiner has rejected claims 8-13 under 35 U.S.C. 103(a) over Sooknanan *et al.* as applied to claims 1 and 3-7 of the instant claims, and further in view of Kwoh *et. al.* and Goller *et. al.* Applicants respectfully traverse this rejection.

For the reasons listed above, Sooknanan *et. al.* fails to teach all of the limitations of claim 1. Kwoh *et. al.* and Goller *et. al.* do not remedy the deficiencies of Sooknanan

*et. al.* . Both Goller *et al.* and Kwoh *et al.* teach first and second strand cDNA synthesis in a single reaction without a change of buffer conditions by serial addition of reagents between the steps.

***Obviousness Rejection Under 35 U.S.C. §103(a)-Sooknanan et al. in view of Schnipelsky et al.***

Claims 20-21 were rejected under 35 U.S.C. §103(a) over Sooknanan *et al.* as applied to claims 1 and 3-7 above and further in view of Schnipelsky *et al.* (5,229,297). See, paper No. 17 at page 7, paragraph 10. Applicants respectfully traverse this rejection.

For the reasons indicated above, Sooknanan *et al.* fails to teach all of the limitations of claim 1 and Schnipelsky *et al.* fails to remedy the deficiencies of Sooknanan *et al.* as applied to dependent claims 20-21. Schnipelsky *et al.* does not teach amplification of a population of nucleic acids or serial addition of reagents resulting in a change of buffer conditions between steps.

For these reasons and the reasons set forth *supra*, Applicants respectfully request that the rejection of claims under 35 U.S.C. §103(a) be reconsidered and withdrawn.

### CONCLUSION

For these reasons, Applicants believe all pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5768.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

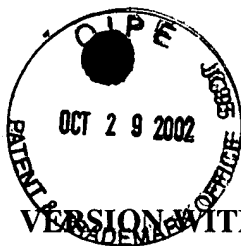
Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES  
MADE TO THE CLAIMS

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*In the Claims*

Please amend Claim 1 as follows:

1. (twice amended) A method for the amplification of a population of nucleic acids comprising a population of poly(A)+ RNA, said method comprising:

a first step of mixing said population of nucleic acids with a primer comprising oligo-dT in a single reaction vessel under conditions that allow hybridization of said primer with said population of poly(A)+ RNA;

a second step of synthesizing a single-stranded DNA population from said population of poly(A)+ RNA wherein a reverse transcriptase, dNTPs and a first buffer are added to the single reaction vessel to synthesize said single-stranded DNA population;

a third step of synthesizing a population of double-stranded DNA from said [a] single-stranded DNA population wherein a second buffer and a four enzyme-mix comprising a DNA polymerase are [is] added to said single reaction vessel to synthesize said double-stranded cDNA; and

a fourth step of synthesizing [producing] multiple copies of RNA from said double-stranded DNA population, wherein an RNA polymerase and a third buffer are added to said [amplification occurs in a] single reaction vessel to synthesize said multiple copies of RNA.

20. The method of claim 1, wherein at least one step of [said] synthesizing [and producing comprise] comprises the use of an automated machine.